REMARKS/ARGUMENTS

Status of the claims:

Upon entry of the present amendment, claims 1, 6, 11, and 38 to 41 will be pending in the application and presented for examination. Claims 2, 3, and 5 are herein cancelled without prejudice to further prosecution. Claims 38 to 41 are newly presented for examination herein.

Support for the amendments to the claims:

Claim 1 has been amended to remove the recitals of 'infectious agents having a lipid bilayer' and 'single chain lipid active agent'. Claim 1 has also been amended to set forth a particular embodiment wherein the method is used to prevent an infection caused by an enveloped virus. Support for this amendment can be found, for example, in claim 4 as originally filed. Finally, claim 1 has been amended to set forth a particular embodiment wherein the active agent is a fatty acid monoglyceride. Support for this amendment can be found, for example, in paragraph [0042] of the specification.

Claim 6 has been amended in order to properly update dependency upon independent claim 1.

Claim 38 is newly presented in order to set for a particular embodiment of the invention wherein the C_2-C_{18} alkyl group is a C_6-C_{12} alkyl group. Support for this amendment can be found, for example, in paragraph [0042] of the specification.

Claim 39 is newly presented in order to set forth a particular embodiment of the invention wherein the fatty acid monoglyceride is 1-O-octyl-sn-glycerol or 2-O-octyl-sn-glycerol. Support for this amendment can be found, for example, in paragraph [0044] of the specification.

Claim 40 is newly presented in order to set forth particular viral agents. Support for this amendment can be found, for example, in claims 5 and 6 as originally filed.

Claim 41 is newly presented in order to set forth particular embodiments of the current formulation. Support for this amendment can be found, for example, in claim 11 as originally filed.

Accordingly, Applicants submit that no new material has been added in the amendments to the claims and respectfully request their entry.

I. Rejections Under 35 U.S.C. §112

1. First Rejection Under 35 U.S.C. §112, First Paragraph

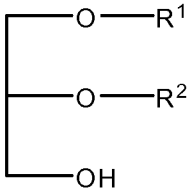
Claims 1-3, 5-6, and 11 stand rejected as allegedly failing to comply with the written description requirement. In this regard, the Examiner has alleged that there is no support for the recital of "infectious agents having a lipid bilayer". Without acquiescing to the merits of the rejection, Applicants have amended the claims in order to remove the recital of "infectious agents having a lipid bilayer". Accordingly, Applicants submit that the claims are no longer subject to the above rejection and respectfully request that this rejection be reconsidered and withdrawn.

2. Second Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-3, 5-6, and 11 stand rejected as allegedly lacking enablement. In this regard, the Examiner has alleged that the specification does not reasonably provide enablement for the generic phrases 'single chain lipid active agent' and prevention of infection. To the extent that the rejection is applicable to the currently amended claim set, Applicants respectfully traverse the rejection.

In an earnest attempt to expedite prosecution, and without acquiescing to the merits of the rejection, Applicants have amended pending independent claim 1 to remove the recital of a 'single chain lipid active agent'. Accordingly, independent claim 1 now recites:

> *A method for preventing a **viral infection** in a mammal, said method comprising: administering a pharmaceutically effective amount of a liposomal formulation to said mammal, wherein said liposomal formulation comprises:*
>
> *a) a lipid vesicle; and*
>
> *b) **a fatty acid monoglyceride of formula:***



wherein* R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen*;* *and,
wherein said viral infection is caused by an ***enveloped virus****.*

Applicants point out that the claims are now drawn to preventing only viral infections with a liposomal composition comprising a fatty acid monoglyceride of the above formula. Accordingly, Applicants respectfully submit that the amended claim set is no longer subject to the above rejection.

As the Examiner points out, the Forman factors dictate whether a disclosure meets the enablement requirements of 35 U.S.C. §112, first paragraphs. These factors include (i) the relative skill of those in the art; (ii) the nature of the invention; (iii) the breadth of the claims; (iv) the amount of guidance presented; (v) the presence of working examples; (vi) the state of the art; (vii) the predictability of the art; and (viii) the quantity of experimentation necessary. *Ex parte Forman*, 230 U.S.P.Q. 546 (PTO Bd. Pat. App. & Inter. 1986), *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). Applicants address these factors as raised by the Examiner. A general summary of the analysis is presented at the conclusion of these remarks.

(i) Nature of the Invention: The invention is drawn to methods for preventing a viral infection caused by an enveloped virus using a liposomal formulation of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen. As the specification clearly describes such fatty acid monoglyceride compounds as used in the claimed methods, Applicants respectfully submit that the invention is enabled with respect to the currently amended claim set.

(ii) State of the Prior Art: Applicants agree with the Examiner that the state of the prior art is very high for formulating liposomal compositions containing specific drugs for the treatment of disease. However, Applicants also submit that the state of the prior art is very high for treating different diseases, sharing a common feature, with the same drug. For example,

TNF-α blockers are used to treat a number of different diseases including, but not limited to, rheumatoid arthritis, psoriatic arthritis, psoriasis, ankylosing spondylitis, Crohn's disease, and ulcerative colitis. As amended, independent claim 1 recites methods for preventing infections caused by ***only*** enveloped viruses. as such the infections cannot be caused by any microorganism. Additionally, Applicants respectfully disagree with the Examiner's argument that treating diseases with a common feature and preventing infections caused by agents having a common feature are sufficiently different as to render the prior art as not enabling. Applicants submit that both processes rely on the exploitation of a common feature. Much like TNF-α blockers, which exploit the action of TNF-α in a variety of diseases, the current invention as claimed prevents viral infections by exploiting viruses that are all enveloped. Therefore, the state of the prior art is clearly enabling for the use of the full scope of the invention as presently claimed.

(iii) Relative Skill of those in the Art: The relative skill of those in the art is very high and is commensurate with Ph.D. level technology as admitted by the Examiner. Therefore, as methods of practicing the current invention as claimed would be routine for one of relative skill in the art, this factor is clearly enabling for the invention as claimed.

(iv) Predictability of the Art: Applicants note that the claims have been significantly narrowed by the amendments. Specifically, the claims are no longer drawn towards methods of preventing infection by any microorganism, rather they are now drawn to preventing infections by enveloped viruses only. Furthermore, the claims no longer recite the use of any single chain lipid, rather they are focused on a narrow set of fatty acid monoglycerides, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen.

The general predictability of formulating liposomally encapsulated compositions is very high as admitted by the Examiner. However, Applicants respectfully disagree with the Examiner's analysis of the lack of predictability when using an effective drug on a novel target. Evidence of such predictability can again be found in the use of TNF-α blockers in the treatment of various diseases sharing a common feature. As in the use of TNF-α blockers, which target

over-induced inflammatory responses, the instant invention also exploits a common feature shared by the viruses, namely that they are all enveloped.

Examples set forth by the Examiner, drawn towards allegedly showing a lack of predictability in the art, are not applicable in the instant case. The Examiner uses the example of a drug-resistant tuberculosis strain as evidence for his argument. Applicants respectfully contend that this example is not material as these drugs target essential tuberculosis proteins, as opposed to viral envelopes as in the instant invention. The cited drug resistance is achieved by introducing mutations in the targeted proteins, resulting in reduced binding affinities for the drugs. This is not the case in the instant invention as the lipids composing the viral envelopes are not encoded by genomic material. Furthermore, the Examiner cites the Zips art as allegedly evidencing that in vitro studies may or may not be enough to predict a compound's effect in vivo. This reference is also immaterial as it is drawn to studies of anticancer agents, which target proteins and nucleic acids, but again not lipid structures.

Therefore, as the art is clearly predictable for liposomal formulations, as well as for the exploitation of common features in molecular biology, the prior art clearly enables one of skill in the art to practice the full scope of the invention as presently claimed.

(v) Breadth of the Claims: In light of the recent amendments, Applicants respectfully submit that the claims are sufficiently narrow. The currently pending claims are drawn to methods of preventing infections by a subclass of viruses, enveloped, with a liposomal formulation of a select set of compounds, fatty acid monoglycerides wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen.

The Examiner alleges that since RNA and DNA viruses each act by different mechanisms at any time, it would be impossible to determine when the individual will be exposed to any specific microbial agent and prevent such subsequent infection. However, Applicants contend that since all relevant DNA and RNA viruses are encapsulated at the point of infection, these viruses would ***all*** necessarily be exposed to the inventive formulations at the time of infection.

Therefore, as the amended claims have been substantially narrowed, the breath of the claims is sufficiently clear as to enable one skilled in the art to practice the full scope of the invention as claimed.

(vi) Amount of Guidance Provided: Applicants note that the claims are drawn to preventing infections by enveloped viruses and not to preventing disease states as alleged by the Examiner. The amount of guidance provided by the specification is high. The specification teaches preferred liposomal formulations, for example, at paragraphs [0029] to [0034]. The specification teaches preferred active agents, for example, at paragraphs [0035] to [0044]. The specification teaches additional agents which can be used in conjunction with the current invention, for example, at paragraphs [0045] to [0046]. The specification teaches modes of administration, for example, at paragraphs [0047] to [0056]. The specification teaches the construction of liposomes, for example, at paragraphs [0057] to [0065]. The specification provides examples of liposomal formulations that are effective in killing gonococcus, HSV-1, HSV-2, and HIV in Examples 1 and 2 at pages 16 to 18. The specification provides an example of administration of a liposomal formulation in Example 3 at pages 18 to 19.

As evidenced above, the specification provides more than ample guidance to enable one skilled in the art to practice the full scope of the invention commensurate in scope with the amended claims.

(vii) Presence of Working Examples: As evidenced above, the specification provides examples of the efficacy of a fatty acid monoglyceride as claimed, octylglycerol, for killing several enveloped viruses, *i.e.*, HSV-1, HSV-2, and HIV. These examples evidence that fatty acid monoglycerides as presently claimed can kill representative agents as recited in the amended claims. Furthermore, the specification teaches that octylglycerol is effective in killing other agents that contain similar outer membrane structures, such as gonococcus, evidencing that the inventive formulation is enabled for more than just enveloped viruses.

The Examiner has alleged that the instant specification provides no working examples as to how the diseases can be prevented using the claimed formulation. Applicants respectfully submit that the Examiner is applying a standard for enablement that is higher than that required by 35 U.S.C. §112, first paragraph. "It is not a requirement of patentability that an

inventor correctly set forth, or even know, how or why the invention works." Newman v. Quigg, 877 F.2d 1575, 1581 (Fed. Cir. 1989). Furthermore, the claims are merely drawn to preventing infections by enveloped viruses, not to preventing disease states.

Applicants submit that the demonstration of the *in vitro* efficacy of a representative species, octylglycerol, for use on a number of representative enveloped viruses, HSV-1, HSV-2, and HIV, is more than sufficient as enabling working examples. The Federal Circuit Court of Appeals has addressed the description required to show one of skill in the art that the inventors were in possession of a claimed genus at the time of filing. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). *An applicant may also show that an invention is complete by...disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention ...i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Id.* at 1613.

Furthermore, "description of a ***representative number*** of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.*, 66 Fed. Reg. 1099, 1106 (2001). "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). M.P.E.P. 2163.

The *in vitro* examples provided in the specification adequately demonstrate the inventive formulations' efficacy for preventing the infection of a number of harmful viruses. Furthermore, as the point of preventing infection occurs *ex vivo*, these studies replicate with some accuracy the conditions under which the formulations would act when applied to a patient.

Therefore, Applicants respectfully submit that the presence of working examples in the specification is enabling for the use of the full scope of the invention as claimed.

(viii) Quantity of Experimentation Necessary: As discussed above, the pending claims have been dramatically narrowed to recite methods for preventing infection by only enveloped viruses through the use of a liposomal formulation of a specific class of fatty acid monoglycerides, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen. Given the limited scope of the amended claims, the presence of working examples, and the detailed description of the claimed formulations in the specification, Applicants respectfully submit that the quantity of experimentation necessary to practice the full scope of the invention as claims is insignificant. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Thus, the quantity of experimentation necessary is sufficiently small to enable one skilled in the art to practice the full scope of the invention as claimed.

Conclusion: In light of the current amendments to the claims and the above analysis of the Forman factors, Applicants respectfully submit that any person skilled in the art to which it pertains, or with which it is most nearly connected to, is enabled to use the full scope of the invention as claimed. As such, Applicants respectfully request that this rejection be reconsidered and withdrawn.

3. First Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1-3, 5-6, and 11 stand rejected as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. In this regard, the Examiner has alleged that the specification does not adequately teach as to what agents have lipid bilayers. Without acquiescing on the merits of the rejection, Applicants have amended the claims in order to remove the recital of "infectious agents having a ***lipid bilayer***". Accordingly, Applicants submit that the claims are no longer subject to the above rejection and respectfully request that this rejection be reconsidered and withdrawn.

II. Rejections Under 35 U.S.C. §102(b)

1. First Rejection Under 35 U.S.C. §102(b)

Claims 1-3, 5-6, and 11 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Hostetler et al. (US 2001/0033862). In this regard, the Examiner has alleged that Hostetler et al. teach liposomal formulations containing single chain lipids for the

inactivation of the HIV virus. To the extent that the rejection is applicable to the currently amended claim set, Applicants respectfully traverse the rejection.

Without acquiescing on the merits of the rejection, Applicants have amended independent claim 1 in order to point out a particular embodiment of the invention, specifically a method of preventing infection with a liposomal formulation of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen. Accordingly, Applicants respectfully submit that Hostetler et al. do not teach a liposomal formulation as recited in the currently amended claims. Thus, Applicants submit that the claims are no longer subject to the above rejection and respectfully request that this rejection be reconsidered and withdrawn.

2. Second Rejection Under 35 U.S.C. §102(b)

Claims 1-2, 4-5, and 11 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Spevak et al. (J. Am. Chem. Soc, 1993). In this regard, the Examiner has alleged that Spevak et al. teach the inhibitory effects of influenza virus by liposomes containing a single chain lipid. To the extent that the rejection is applicable to the currently amended claim set, Applicants respectfully traverse the rejection.

Without acquiescing on the merits of the rejection, Applicants have amended independent claim 1 in order to point out a particular embodiment of the invention, specifically a method of preventing infection with a liposomal formulation of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen. As Spevak et al. teach lipid derivatives of *O*-sialosides, not fatty acid monoglycerides, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen, Applicants respectfully submit that Spevak et al. do not teach liposomal formulations as recited in the currently amended claims. Thus, Applicants submit that the claims are no longer subject to the above rejection and respectfully request that this rejection be reconsidered and withdrawn.

III. Rejection Under 35 U.S.C. §103(a)

Pending claims 1-6 and 11 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Eibl (US 2002/0173489) in combination with Ho et al. (US 2004/0208921), Hostetler et al. (US2001/0033862) and Firshein (U.S. Patent No. 6,121,245), individually or in combination. In this regard, the Examiner alleges that Eibl teaches formulations containing

single chain lipids for infections such as HIV. The Examiner further alleges that Ho et al., Hostetler et al., and Firshein teach the use of liposomes as delivery agents for such drugs. To the extent that the rejection is applicable to the currently amended claim set, Applicants respectfully traverse the rejection.

NO PRIMA FACIE CASE OF OBVIOUSNESS EXISTS

Applicants respectfully point out that the currently amended claims are focused on methods of using liposomal formulations of fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen for the prevention of viral infections. As such, Applicants respectfully assert that a *prima facie* case of obviousness has not been established for the presently claimed invention. To establish a *prima facie* case of obviousness, three basic criteria must be met:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully submit that a *prima facie* case of obviousness has not been established because the cited references do not teach all the claimed limitations. Specifically, Applicants assert that none of the cited references teach the use of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen for the prevention of viral infections. Applicants address each of the cited references below.

The Eibl reference teaches the use of a medicament in which the active ingredient is a phosphorus containing compound as evidenced in paragraph [0011] of the Eibl specification, reproduced here for the Examiner's convenience:

> *These objects are achieved via a medicament which contains* ***as active material*** *at least one compound of the formula* $R\text{-}Y\text{-}P^{O}{}_{2}\text{-}X\text{-}R_1$
> [Emphasis added]

As such, the Eibl reference ***does not*** teach the use of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen for the prevention of viral infection. Eibl merely teaches the use of alkylglycerols ***in combination*** with the active ingredient as described above. The following passage can be found at paragraph [0049] of the Eibl specification:

> *It has proved to be especially favorable to use the compounds of the formula I and I' **together** with at least one alkylglycerol*...[Emphasis added]

As such, the Eibl reference does not teach liposomal formulations as claimed in the amended claim set for the prevention of infection. Furthermore, Applicants submit that Eibl does not teach the prevention of viral infections at all. As admitted by the Examiner in the Office Action dated February 21, 2008, the methods taught by Eibl are drawn to preventing proliferation and not to preventing infection.

> *Finally, since viruses such as HIV remain **dormant** and the antiviral agents actually prevent **proliferation** of the virus*... [Emphasis added]

The Examiner's passage clearly teaches that the HIV virus has already infected the individual, as ***dormancy*** and ***proliferation*** occur *in vivo*. Applicants respectfully remind the Examiner that the methods of the pending claims are drawn to ***preventing infection***, a process which occurs *ex vivo* and clearly before a virus has the opportunity to become dormant ***inside of a cell***. As such, Applicants respectfully assert that Eibl does not teach the use of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen ***by itself*** and furthermore, does not teach methods for the ***prevention*** of infection at all.

Similarly, Hostetler et al., as outlined above, also fail to teach the use of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen in the prevention of viral infections. Furthermore, neither the Ho *et al.* nor the Firshein references supplement this deficiency. Firshein, while teaching that alkylglycerols can be administered in liposomal formulations, is drawn to methods for treating malignant tumors and not for preventing viral infections. Finally, Ho et al., as admitted by the Examiner, disclose liposomal

formulations of drugs for targeted delivery to lymphoid tissues. However, Ho et al. do not teach the use of a fatty acid monoglyceride, wherein R^1 or R^2 is a C_2-C_{18} alkyl group and the other is hydrogen for the prevention of viral infections. Therefore, as this reference also fails to supplement the deficiencies of the Eibl art, the combination of the cited references fails to teach or suggest all the claim limitations of the instant claims. As such, Applicants assert that no *prima facie* case of obviousness exists and respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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